METHOD AND APPARATUS FOR DETERMINING
ALTERNANS DATA OF AN ECG SIGNAL

BACKGROUND OF THE INVENTION

[0001]   The present invention relates to cardiology, and more specifically to methods and apparatus for determining alternans data of an electrocardiogram ("ECG") signal.

[0002]   Alternans are a subtle beat-to-beat change in the repeating pattern of an ECG signal. Several studies have demonstrated a high correlation between an individual's susceptibility to ventricular arrhythmia and sudden cardiac death and the presence of a T-wave alternans ("TWA") pattern of variation in the individual's ECG signal.

[0003]   While an ECG signal typically has an amplitude measured in millivolts, an alternans pattern of variation with an amplitude on the order of a microvolt may be clinically significant. Accordingly, an alternans pattern of variation is typically too small to be detected by visual inspection of the ECG signal in its typical recorded resolution. Instead, digital signal processing and quantification of the alternans pattern of variation is necessary. Such signal processing and quantification of the alternans pattern of variation is complicated by the presence of noise and time shift of the alternans pattern of variation to the alignment points of each beat, which can be caused by limitation of alignment accuracy and/or physiological variations in the measured ECG signal. Current signal processing techniques utilized to detect TWA patterns of variation in an ECG signal include spectral domain methods and time domain methods.

BRIEF DESCRIPTION OF THE INVENTION

[0004]   In light of the above, a need exists for a technique for detecting TWA patterns of variation in an ECG signal that provides improved performance as a stand-alone technique and as an add-on to other techniques. Accordingly, one or more embodiments of the invention provide methods and apparatus for determining alternans data of an ECG signal. In some embodiments, the method can include determining at least one value representing at least one morphology feature of each beat of the ECG signal and generating a set of data points based on a total quantity of values and a total quantity of beats. The data points can each include a first value determined using a first mathematical function and a second value determined using a second mathematical function. The method can also include separating

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the data points into a first group of points and a second group of points and generating a feature map by plotting the first group of points and the second group of points in order to assess an alternans pattern of variation.

BRIEF DESCRIPTION OF THE DRAWINGS

[0005]   FIG. 1 is a schematic diagram illustrating a cardiac monitoring system according to the invention.

[0006]   FIG. 2 illustrates an ECG signal.

[0007]   FIG. 3 is a flow chart illustrating one embodiment of a method of the invention.

[0008]   FIG. 4 illustrates a maximum morphology feature.

[0009]   FIG. 5 illustrates a minimum morphology feature.

[0010]   FIG. 6 illustrates an area morphology feature.

[0011]   FIG. 7 illustrates another area morphology feature.

[0012]   FIG. 8 illustrates a further area morphology feature.

[0013]   FIG. 9 illustrates still another area morphology feature.

[0014]   FIG. 10 illustrates a plurality of beats, each beat being divided into a plurality of portions.

[0015]   FIG. 11 illustrates a window establishing a size of one of the plurality of portions of FIG. 10.

[0016]   FIG. 12 illustrates a feature matrix.

[0017]   FIG. 13 illustrates a decomposition of the feature matrix of FIG. 12 as generated by a principal component analysis.

[0018]   FIG. 14 illustrates a plot of values of data corresponding to values representative of a morphology feature.

[0019]   FIG. 15 illustrates a determination of difference features using the values plotted in FIG. 14.

[0020]   FIG. 16 illustrates another determination of difference features using the values plotted in FIG. 14.

[0021]   FIG. 17 illustrates a further determination of a difference feature using the values plotted in FIG. 14.

[0022]   FIG. 18 illustrates a feature map of first and second groups of points generated using values of a vector of data.

[0023]   FIG. 19 illustrates a feature map generated using values of a vector of data generated by performing a principal component analysis on a feature matrix including the vector of data utilized to generate the feature map of FIG. 18.

[0024]   FIG. 20 illustrates a feature map of first and second groups of points generated using a first mathematical function and a second mathematical function.

[0025]   FIG. 21 illustrates a feature map of third and fourth groups of points generated using a third mathematical function and a fourth mathematical function.

[0026]   FIG. 22 illustrates a feature map of fifth and sixth groups of points generated using a fifth mathematical function and the sixth mathematical function.

[0027]   FIG. 23 illustrates a distance between a first center point of a first group of points and a second center point of a second group of points each plotted to form a feature map.

[0028]   FIG. 24 illustrates a spectral graph generated using values of a vector of data.

[0029]   FIG. 25 illustrates a spectral graph generated using values of a vector of data generated by performing a principal component analysis on a feature matrix including the vector of data utilized to generate the spectral graph of FIG. 24.

DETAILED DESCRIPTION

[0030]   Before any embodiments of the invention are explained in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of components set forth in the following description or illustrated in the

following drawings. The invention is capable of other embodiments and of being practiced or of being carried out in various ways. Also, it is to be understood that the phraseology and terminology used herein is for the purpose of description and should not be regarded as limited. The use of "including," "comprising" or "having" and variations thereof herein is meant to encompass the items listed thereafter and equivalents thereof as well as additional items. The terms "mounted," "connected" and "coupled" are used broadly and encompass both direct and indirect mounting, connecting and coupling. Further, "connected" and "coupled" are not restricted to physical or mechanical connections or couplings, and can include electrical connections or couplings, whether direct or indirect.

[0031] In addition, it should be understood that embodiments of the invention include both hardware and electronic components or modules that, for purposes of discussion, may be illustrated and described as if the majority of the components were implemented solely in hardware. However, one of ordinary skill in the art, and based on a reading of this detailed description, would recognize that, in at least one embodiment, the electronic based aspects of the invention may be implemented in software. As such, it should be noted that a plurality of hardware and software based devices, as well as a plurality of different structural components may be utilized to implement the invention. Furthermore, and as described in subsequent paragraphs, the specific mechanical configurations illustrated in the drawings are intended to exemplify embodiments of the invention and that other alternative mechanical configurations are possible.

[0032] FIG. 1 illustrates a cardiac monitoring system 10 according to some embodiments of the invention. The cardiac monitoring system 10 can acquire ECG data, can process the acquired ECG data to determine alternans data, and can output the alternans data to a suitable output device (e.g., a display, a printer, and the like). As used herein and in the appended claims, the term "alternans data" includes TWA data, or any other type of alternans data that is capable of being determined using one or more embodiments of the invention.

[0033] The cardiac monitoring system 10 can acquire ECG data using a data acquisition module. It should be understood that ECG data can be acquired from other sources (e.g., from storage in a memory device or a hospital information system). The data acquisition module can be coupled to a patient by an array of sensors or transducers which may include, for example, electrodes coupled to the patient for obtaining an ECG signal. In the illustrated embodiment, the electrodes can include a right arm electrode RA; a left arm electrode LA;

chest electrodes V1, V2, V3, V4, V5 and V6; a right leg electrode RL; and a left electrode leg LL for acquiring a standard twelve-lead, ten-electrode ECG. In other embodiments, alternative configurations of sensors or transducers (e.g., less than ten electrodes) can be used to acquire a standard or non-standard ECG signal.

[0034] A representative ECG signal is schematically illustrated in FIG 2. The ECG signal can include [G] beats including beat-one B_1 through beat-[G] B_G where [G] is a value greater than one. As used herein and in the appended claims, a capital letter in brackets represents a quantity, and a capital letter without brackets is a reference character (similar to a typical reference numeral).

[0035] The data acquisition module can include filtering and digitization components for producing digitized ECG data representing the ECG signal. In some embodiments, the ECG data can be filtered using low pass and baseline wander removal filters to remove high frequency noise and low frequency artifacts. The ECG data can, in some embodiments, be filtered by removing arrhythmic beats from the ECG data and by eliminating noisy beats from the ECG data.

[0036] The cardiac monitoring system 10 can include a processor and a memory associated with the processor. The processor can execute a software program stored in the memory to perform a method of the invention as illustrated in FIG. 3. FIG. 3 is a flow chart of a method of the invention used to determine and display alternans data of an ECG signal. Although the cardiac monitoring system 10 is described herein as including a single processor that executes a single software program, it should be understood that the system can include multiple processors, memories, and/or software programs. Further, the method of the invention illustrated in FIG. 3 can be performed manually or using other systems.

[0037] As shown in FIG. 3, the processor can receive (at 100) ECG data representing an ECG signal. The acquired ECG data can be received (e.g., from a patient in real-time via the data acquisition module or from storage in a memory device) and can be processed as necessary. The ECG data can represent continuous and/or non-continuous beats of the ECG signal. In one embodiment, the ECG data, or a portion thereof, can be parsed into a plurality of data sets. Each data set can represent a portion of a respective beat B of the ECG signal (e.g., the T-wave portion of a respective beat B of the ECG signal), a portion of a respective odd or even median beat of the ECG signal, a portion of a respective odd or even mean beat

of the ECG signal, and the like. The parsed data sets can be saved in an array (e.g., a waveform array). In other embodiments, the ECG data can be saved in a single data set, or alternatively, saved in multiple data sets.

[0038] The processor can determine (at 102) a quantity [C] of values W representing a quantity [D] of morphology features F of a beat B (e.g., beat-one B_1) of a quantity [G] beats, where [C] and [D] are each a quantity greater than or equal to one. In some embodiments, a single value W is determined for each morphology feature F (i.e., the quantity of [C] is equal to the quantity of [D]). However, in some embodiments, multiple values W are determined for a single morphology feature F and/or a single value W is determined for multiple morphology features F. Determining a quantity [C] of values W representing a quantity [D] of morphology features F can be repeated for a quantity [H-1] of beats of the quantity [G] of beats represented in the collected ECG data where a quantity [H] is greater than or equal to one and less than or equal to the quantity [G].

[0039] In some embodiments, any morphology features F of the beats B can be determined. FIGS. 4-9 illustrate some examples of such morphology features F. FIG. 4 illustrates a maximum morphology feature (i.e., the maximum value of the data set representing the T-wave portion of a respective beat). FIG. 5 illustrates a minimum morphology feature (i.e., the minimum value of the data set representing the T-wave portion of a respective beat). FIG. 6 illustrates an area morphology feature (i.e., the area between a curve formed by the data set representing the T-wave portion of a respective beat and a baseline established by the minimum value of the data set). FIG. 7 illustrates another area morphology feature (i.e., the area between a curve formed by the data set representing the T-wave portion of a respective beat and a baseline established by the maximum value of the data set and a point of the data set representing the maximum up-slope of the curve). FIG. 8 illustrates still another area morphology feature (i.e., the area between a curve formed by the data set representing the T-wave portion of a respective beat and a baseline established by the minimum value of the data set and a point of the data set representing the maximum down-slope of the curve). FIG. 9 illustrates yet another area morphology feature (i.e., the area between a curve formed by the data set representing the T-wave portion of a respective beat and a baseline established by a point of the data set representing the maximum up-slope of the curve and a point of the data set representing the maximum down-slope of the curve). Other types of maximum, minimum, and area morphology features can also be used.

[0040]   Other examples of morphology features that can be used include amplitude morphology features (e.g., an amplitude of a point representing the maximum down-slope of the curve formed by the data set representing the T-wave portion of a respective beat) and slope morphology features (e.g., a maximum positive slope of the curve formed by the data set representing the T-wave portion of a respective beat). Another example is mathematical model morphology features obtained by determining values representing a mathematical model of the curve formed by the data set representing the T-wave portion of a respective beat using, for example, a Gaussian function model, a power of Cosine function model, and/or a bell function model. A further example is time interval morphology features (e.g., a time interval between a maximum value and a minimum value of the data set representing a T-wave portion of a respective beat). Still another example is shape correlation morphology features obtained by determining a value representing a shape correlation of the curve formed by the data set representing the T-wave portion of a respective beat using, for example, a cross-correlation method and/or an absolute difference correlation method. An additional example is ratio morphology features (e.g., a ST:T ratio). Any other suitable morphology feature can be used in other embodiments of the invention. In some embodiments, as discussed above, the morphology feature can be determined using values of the data set(s) of the ECG data. In other embodiments, the morphology features can be determined using values representing the values of the data set(s) of the ECG data (e.g., a morphology feature of the first derivative of the curve formed by a respective data set).

[0041]   Morphology features can be determined using an entire parsed data set as illustrated in FIGS. 4-9, or alternatively, using a portion thereof as illustrated in FIGS. 10 and 11. As shown in FIG. 10, each of the beats B can be divided up in a plurality of portions. The center of each portion can be defined by a vertical divider line. As shown in FIG. 11, a window can be established to define the size of the portion. The window can include a single value of the data set (e.g., a value representing the point where the divider line crosses the curve formed by the data set), or values of the data set representing any number of points adjacent the intersection of the curve and the divider line.

[0042]   As shown in FIG. 3, the processor can generate (at 104) a feature matrix. As used herein and in the appended claims, the term "matrix" includes any table of values. The generated feature matrix can include a quantity [C] of values W representing each of the quantity [D] of morphology features F for each of the quantity [H] of beats B (i.e., the feature

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matrix includes a quantity [C]x[H] of values W). Each value W can directly represent the determined morphology feature F (e.g., the actual value of the determined area morphology feature), or can indirectly represent the determined morphology feature (e.g., a normalized value of the determined area morphology feature).

[0043]   A representative column-wise feature matrix A is illustrated in FIG. 12. The feature matrix A can include [C] columns and [H] rows. The feature matrix A can use the columns to represent the quantity [D] of morphology features F (i.e., each column includes a quantity [H] of values W of the same morphology feature as determined for each of the quantity [H] of beats B), and the rows to represent the beats B (i.e., each row includes a quantity [C] of values representing the quantity [D] of morphology features for each of the quantity [H] of beats). The values W of the morphology features F can be represented in the illustrated feature matrix A using the notation W_{IBJ} and $F_{I}B_{J}$ where I is a value between one and [C], the quantity of [C] being equal to the quantity of [D], and J is a value between one and [H]. In other embodiments, the feature matrix A can be arranged in other suitable manners. In yet other embodiments, the values W representing the morphology features F can be saved for later processing.

[0044]   As shown in FIG. 3, the processor can preprocess (at 106) the feature matrix A. In some embodiments, a principal component analysis (PCA) can be performed on the feature matrix A. PCA involves a multivariate mathematical procedure known as an eigen analysis which rotates the data to maximize the explained variance of the feature matrix A. In other words, a set of correlated variables are transformed into a set of uncorrelated variables which are ordered by reducing variability, the uncorrelated variables being linear combinations of the original variables. PCA is used to decompose the feature matrix A into three matrices, as illustrated in FIG. 13. The three matrices can include a matrix U, a matrix S, and a matrix V.

[0045]   The matrix U can include the principal component vectors (e.g., the first principal component vector u_1, the second principal component vector u_2, ..., the pth principal component vector u_p). The principal component vectors are also known as eigen vectors. The first principal component vector u_1 can represent the most dominant variance vector (i.e., the first principal component vector u_1 represents the largest beat-to-beat variance), the second principal component vector u_2 can represent the second most dominant variance vector, and so on.

[0046]   The S Matrix can include the principal components (e.g., the first principal component S_1, the second principal component S_2, ..., the pth principal component S_p). The first principal component S_1 can account for as much of the variability in the data as possible, and each succeeding principal component S can account for as much of the remaining variability as possible. The first principal component S_1 can be used to determine alternans data (e.g., the square-root of the first PCA component S_1 can provide an estimation of the amplitude of the most dominant alternans pattern of variation). In some embodiments, the second principal component S_2 and the third principal component S_3 can also provide useful alternans data.

[0047]   The matrix V is generally known as the parameter matrix. The matrix V can be raised to a power of T. In other embodiments, the preprocessing of the feature matrix A can include other types of mathematical analyses.

[0048]   The robustness of the preprocessing of the feature matrix A can be enhanced by increasing the quantity of [H] as the quantity of [D] increases. In other words, an increase in the number of morphology features F represented in the feature matrix A generally requires a corresponding increase in the number of beats B for which the morphology features F are being determined. The correspondence between the quantities of [D] and [H] is often based on the dependency between each of the [D] morphology features F. In some embodiments, the quantity of [H] is greater than or equal to 32 and less than or equal to 128. In other embodiments, the quantity of [H] is less than 32 or greater than 128. In some embodiments, the value of [H] is adaptively changed in response to a corresponding change in the level of noise in the measured ECG signal.

[0049]   As shown in FIG. 3, the processor can determine (at 108) [E] points L using data corresponding to at least some of the values W, [E] being a quantity greater than or equal to one. The data corresponding to the values W can include at least one value W, at least one value of a principal component vector (e.g., the first principal component vector u_1), and/or at least one value of any other data that corresponds to the values W. Each point L can include a first value (e.g., one of an X-value and a Y-value) determined using a first mathematical function Feature(beat+[N]), and a second value (e.g., the other of the X-value and the Y-value) determined using a second mathematical function Feature(beat), [N] being a quantity greater than or equal to one. Each of the first and second values of the points L represents a feature of the data corresponding to the values W. In the illustrated embodiment, the feature

is a difference feature Q (i.e., the difference in amplitude between two values of the data corresponding to the values W as specified by the respective mathematical function). In other embodiments, the first and second values of the points L can represent another difference features (e.g., an absolute difference feature, a normalized difference feature, a square-root difference feature, and the like), or any other mathematically-definable feature of the data corresponding to the values W. For example, the feature can include a value feature where the feature is equal to a specified value of the data corresponding to the determined values W.

[0050]   Equations 1 and 2 shown below define an example of the mathematical functions Feature(beat+[N]) and Feature(beat), respectively. The first values of the points L determined using the mathematical function Feature(beat+[N]) can represent a difference feature $Q_{K+[N]}$ and the second values of the points L determined using the mathematical function Feature(beat) can represent the difference feature Q_K, where K is a value equal to a beat (i.e., the beat for which the respective mathematical function is being used to determine either the first or second value of a point L).

[e1] $\text{Feature}(\text{beat} + [N]) = W_{(\text{beat}+2[N])} - W_{(\text{beat}+[N])} = Q_{K+[N]}$

[e2] $\text{Feature}(\text{beat}) = W_{(\text{beat}+[N])} - W_{(\text{beat})} = Q_K$

[0051]   Tables 1-3 shown below represent the determination of points L using the mathematical functions Feature(beat+[N]) and Feature(beat) as defined in Equations 1 and 2 for [N]=1, 2, and 3, respectively. Equations 3 and 4 shown below define the mathematical functions Feature(beat+[N]) and Feature(beat) for [N]=1.

[e3] $\text{Feature}(\text{beat} + 1) = W_{(\text{beat}+2)} - W_{(\text{beat}+1)} = Q_{K+1}$

[e4] $\text{Feature}(\text{beat}) = W_{(\text{beat}+1)} - W_{(\text{beat})} = Q_K$

Equations 5 and 6 shown below define the mathematical functions Feature(beat+[N]) and Feature(beat) for [N]=2.

[e5] $Feature(beat + 2) = W_{(beat+4)} - W_{(beat+2)} = Q_{K+2}$

[e6] $Feature(beat) = W_{(beat+2)} - W_{(beat)} = Q_K$

Equations 7 and 8 shown below define the mathematical functions Feature(beat+[N]) and Feature(beat) for [N]=3.

[e7] $Feature(beat + 3) = W_{(beat+6)} - W_{(beat+3)} = Q_{K+3}$

[e8] $Feature(beat) = W_{(beat+3)} - W_{(beat)} = Q_K$

[0052]   As shown by Equations 3-8, the offset between the difference feature $Q_{K+[N]}$ and the difference feature Q_K is dependent on the value of [N]. For [N]=1, the first value of the point L is determined by finding the difference between the value W of the second next beat B_{I+2} and the value W of the next beat B_{I+1}, while the second value of the point L is determined by finding the difference between the value W of the next beat B_{I+1} and the value W of the current beat B_I. For [N]=2, the first value of the point L is determined by finding the difference between the value W of the fourth next beat B_{I+4} and the value W of the second next beat B_{I+2}, while the second value of the point L is determined by finding the difference between the value W of the second next beat B_{I+2} and the value W of the current beat B_I. For [N]=3, the first value of the point L is determined by finding the difference between the value W of the sixth next beat B_{I+6} and the value W of the third next beat B_{I+3}, while the second value of the point L is determined by finding the difference between the value W of the third next beat B_{I+3} and the value W of the current beat B_I. Accordingly, the first values of the points L determined using the first mathematical function Feature(beat+[N]) are offset relative to the second values of the points L determined using the second mathematical function Feature(beat) by a factor of [N]. For example, for [N]=1, the first mathematical function Feature(beat+[N]) determines Feature(2) ... Feature(Z+1) for beat-one B_1 through beat-(Z) B_Z, while the second mathematical function Feature(beat) determines Feature(1) ... Feature(Z) for beat-one B_1 through beat-(Z) B_Z; for [N]=2, the first mathematical function Feature(beat+[N]) determines Feature(3) ... Feature(Z+2) for beat-one B_1 through beat-(Z) B_Z, while the second mathematical function Feature(beat) determines Feature(1) ...

Feature(Z) for beat-one B_1 through beat-(Z) B_Z; for [N]=3, the first mathematical function Feature(beat+[N]) determines Feature(4) ... Feature(Z+3) for beat-one B_1 through beat-(Z) B_Z while the second mathematical function Feature(beat) determines Feature(1) ... Feature(Z) for beat-one B_1 through beat-(Z) B_Z. This offset relationship between the first values of the points L determined using the first mathematical function Feature(beat+[N]) and the second values of the points L determined using the second mathematical function Feature(beat) is further illustrated in Tables 1-3.

[0053]   In Tables 1-3 shown below, the "Beat" column can represent respective beats B of the ECG signal and the "Feature Value" column can represent a value W of a morphology feature F of the corresponding respective beat B (e.g., an area morphology feature). As discussed above, the points L can be generated using values of other data corresponding to the determined values W. Also in Tables 1-3, an asterisk (*) represents an undetermined value of the point L (i.e., a value of the point L for which feature values W corresponding to beats B subsequent to the listed beats B_1-B_{12} are required to determine the value of the point L), "f(b+N)" represents the mathematical function Feature(beat+[N]), and "f(b)" represent the mathematical function Feature(beat). Each point L shown in Tables 1-3 includes an X-value determined using the first mathematical function Feature(beat+[N]) and a Y-value determined using the second mathematical function Feature(beat).

[t1]

Beat	Feature Value	[N]=1				Feature Map	
		$f(b+N)=W_{(b+2N)}-W_{(b+N)}$ $f(b+1)=W_{(b+2)}-W_{(b+1)}$		$f(b)=W_{(b+N)}-W_{(b)}$ $f(b)=W_{(b+1)}-W_{(b)}$		Point	Group
1	2	f(2)=3-5=	-2	f(1)=5-2=	3	(-2,3)	A
2	5	f(3)=6-3=	3	f(2)=3-5=	-2	(3,-2)	B
3	3	f(4)=2-6=	-4	f(3)=6-3=	3	(-4,3)	A
4	6	f(5)=4-2=	2	f(4)=2-6=	-4	(2,-4)	B
5	2	f(6)=3-4=	-1	f(5)=4-2=	2	(-1,2)	A
6	4	f(7)=7-3=	4	f(6)=3-4=	-1	(4,-1)	B
7	3	f(8)=3-7=	-4	f(7)=7-3=	4	(-4,4)	A
8	7	f(9)=5-3=	2	f(8)=3-7=	-4	(2,-4)	B
9	3	f(10)=3-5=	-2	f(9)=5-3=	2	(-2,2)	A
10	5	f(11)=7-3=	4	f(10)=3-5=	-2	(4,-2)	B
11	3	$f(12)=W_{13}-7=$	*	f(11)=7-3=	4	(*,4)	A
12	7	$f(13)=W_{14}-W_{13}=$	*	$f(12)=W_{13}-7=$	*	(*,*)	B

[t2]

Beat	Feature Value	[N]=2		Feature Map	
		$f(b+N)=W_{(b+2N)}-W_{(b+N)}$ $f(b+2)=W_{(b+4)}-W_{(b+2)}$	$f(b)=W_{(b+N)}-W_{(b)}$ $f(b)=W_{(b+2)}-W_{(b)}$	Point	Group
1	2	$f(3)=2-3=$ -1	$f(1)=3-2=$ 1	(-1,1)	A
2	5	$f(4)=4-6=$ -2	$f(2)=6-5=$ 1	(-2,1)	B
3	3	$f(5)=3-2=$ 1	$f(3)=2-3=$ -1	(1,-1)	A
4	6	$f(6)=7-4=$ 3	$f(4)=4-6=$ -2	(3,-2)	B
5	2	$f(7)=3-3=$ 0	$f(5)=3-2=$ 1	(0,1)	A
6	4	$f(8)=5-7=$ -2	$f(6)=7-4=$ 3	(-2,3)	B
7	3	$f(9)=3-3=$ 0	$f(7)=3-3=$ 0	(0,0)	A
8	7	$f(10)=7-5=$ 2	$f(8)=5-7=$ -2	(2,-2)	B
9	3	$f(11)=W_{13}-3=$ *	$f(9)=3-3=$ 0	(*,*)	A
10	5	$f(12)=W_{14}-7=$ *	$f(10)=7-5=$ 2	(*,*)	B
11	3	$f(13)=W_{15}-W_{13}=$ *	$f(11)=W_{13}-3=$ *	(*,*)	A
12	7	$f(14)=W_{16}-W_{14}=$ *	$f(12)=W_{14}-7=$ *	(*,*)	B

[t3]

Beat	Feature Value	[N]=3		Feature Map	
		$f(b+N)=W_{(b+2N)}-W_{(b+N)}$ $f(b+3)=W_{(b+6)}-W_{(b+3)}$	$f(b)=W_{(b+N)}-W_{(b)}$ $f(b)=W_{(b+3)}-W_{(b)}$	Point	Group
1	2	$f(4)=3-6=$ -3	$f(1)=6-2=$ 4	(-3,4)	A
2	5	$f(5)=7-2=$ 5	$f(2)=2-5=$ -3	(5,-3)	B
3	3	$f(6)=3-4=$ -1	$f(3)=4-3=$ 1	(-1,1)	A
4	6	$f(7)=5-3=$ 2	$f(4)=3-6=$ -3	(2,-3)	B
5	2	$f(8)=3-7=$ -4	$f(5)=7-2=$ 5	(-4,5)	A
6	4	$f(9)=7-3=$ 4	$f(6)=3-4=$ -1	(4,-1)	B
7	3	$f(10)=W_{13}-5=$ *	$f(7)=5-3=$ 2	(*,*)	A
8	7	$f(11)=W_{14}-3=$ *	$f(8)=3-7=$ -4	(*,*)	B
9	3	$f(12)=W_{15}-7=$ *	$f(9)=7-3=$ 4	(*,*)	A
10	5	$f(13)=W_{16}-W_{13}=$ *	$f(10)=W_{13}-5=$ *	(*,*)	B
11	3	$f(14)=W_{17}-W_{14}=$ *	$f(11)=W_{14}-3=$ *	(*,*)	A
12	7	$f(15)=W_{18}-W_{15}=$ *	$f(12)=W_{15}-7=$ *	(*,*)	B

[0054] FIG. 14 illustrates a plot of the feature values from Tables 1-3 for beat-one B_1 through beat-seven B_7 where each peak and each valley of the plot can represent a respective feature value W (e.g., value-one W_1 which represents beat-one B_1, value-two W_2 which represents beat-two B_2, ..., value-seven W_7 which represents beat-seven B_7).

[0055]   FIG. 15 illustrates for [N]=1 how the mathematical functions Feature(beat+[N]) and Feature(beat) determine the first and second values of the points L which represent the difference features Q_K and Q_{K+1}. For [N]=1, the seven values (i.e., value-one W_1 through value-seven W_7) generate six difference features (i.e., difference feature-one Q_1 through difference feature-six Q_6). Referring to Table 1, the first mathematical function generates difference feature-two Q_2 through difference feature-six Q_6 for beat-one B_1 through beat-five B_5, respectively, using the seven values, and the second mathematical function generates difference feature-one Q_1 through difference feature-six Q_6 for beat-one B_1 through beat-six B_6, respectively, using the seven values.

[0056]   The difference feature Q is illustrated in FIG. 15 as dotted-line arrows extending between two specified values of the plot of FIG. 14. As an example, to determine difference feature-three Q_3 (i.e., the first value of the point L as determined by the first mathematical function Feature(beat+[N]) for beat-two B_2, the second value of the point L as determined by the second mathematical function Feature(beat) for beat-three B_3), the difference can be found between value-four W_4 which represents beat-four B_4 and value-three W_3 which represents beat-three B_3. Similarly, to determine difference feature-six Q_6 (i.e., the first value of the point L as determined by the first mathematical function Feature(beat+[N]) for beat-two B_5, the second value of the point L as determined by the second mathematical function Feature(beat) for beat-six B_6), the difference can be found between value-four W_7 which represents beat-seven B_7 and value-six W_6 which represents beat-six B_6.

[0057]   FIG. 16 illustrates for [N]=2 how the mathematical functions Feature(beat+[N]) and Feature(beat) determine the first and second values of the points L which represent the difference features Q_K and Q_{K+2}. For [N]=2, the seven values (i.e., value-one W_1 through value-seven W_7) generate five difference features (i.e., difference feature-one Q_1 through difference feature-five Q_5). Referring to Table 2, the first mathematical function generates difference feature-three Q_3 through difference feature-five Q_5 for beat-one B_1 through beat-three B_3, respectively, using the seven values, and the second mathematical function generates difference feature-one Q_1 through difference feature-five Q_5 for beat-one B_1 through beat-five B_5, respectively, using the seven values.

[0058]   The difference feature Q is illustrated in FIG. 16 as dotted-line arrows extending between two specified values of the plot of FIG. 14. As an example, to determine difference feature-three Q_3 (i.e., the first value of the point L as determined by the first mathematical

function Feature(beat+[N]) for beat-one B_1, the second value of the point L as determined by the second mathematical function Feature(beat) for beat-three B_3), the difference can be found between value-five W_5 which represents beat-five B_5 and value-three W_3 which represents beat-three B_3. Similarly, to determine difference feature-five Q_5 (i.e., the first value of the point L as determined by the first mathematical function Feature(beat+[N]) for beat-three B_3, the second value of the point L as determined by the second mathematical function Feature(beat) for beat-five B_5), the difference can be found between value-four W_7 which represents beat-seven B_7 and value-five W_5 which represents beat-five B_5.

[0059]   FIG. 17 illustrates for [N]=3 how the mathematical functions Feature(beat+[N]) and Feature(beat) determine the first and second values of the points L which represent the difference features Q_K and Q_{K+3}. For [N]=3, the seven values (i.e., value-one W_1 through value-seven W_7) generate four difference features (i.e., difference feature-one Q_1 through difference feature-four Q_4). Referring to Table 3, the first mathematical function generates difference feature-four Q_4 for beat-four B_4 using the seven values, and the second mathematical function generates difference feature-one Q_1 through difference feature-four Q_4 for beat-one B_1 through beat-four B_4, respectively, using the seven values.

[0060]   The difference feature Q is illustrated in FIG. 17 as dotted-line arrows extending between two specified values of the plot of FIG. 14. As an example, to determine difference feature-three Q_4 (i.e., the first value of the point L as determined by the first mathematical function Feature(beat+[N]) for beat-one B_1, the second value of the point L as determined by the second mathematical function Feature(beat) for beat-three B_3), the difference can be found between value-seven W_7 which represents beat-seven B_7 and value-four W_4 which represents beat-four B_4.

[0061]   As shown by the "Group" column of Tables 1-3, each point L can be assigned to a respective group (e.g., group A or group B). The points L representing each odd beat (e.g., beat-one B_1, beat-three B_3, ..., beat-eleven B_{11}) can be assigned to a first group (i.e., group A), and the points representing each even beat (e.g., beat-two B_2, beat-four B_4, ..., beat-twelve B_{12}) can be assigned to a second group (i.e., group B). The points L can be assigned to group A and group B in this manner to represent a proposed odd-even alternans pattern of variation (i.e., ABAB...). In other embodiments, the points L can be alternatively assigned to groups to represent other proposed alternans patterns of variation (e.g., AABBAABB..., AABAAB..., and the like).

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[0062]   As shown in FIG. 3, the processor can plot (at 110) a feature map [e.g., a feature map of Feature(beat+[N]) versus Feature(beat)]. Both groups of points L (e.g., group A and group B) can be plotted on the same axis to generate the feature map. The polarity of the differences of the group A points are inverted relative to the polarities of the differences of the group B points. As a result, plotting the points L determined using the mathematical functions Feature(beat) and Feature(beat+[N]) as defined by Equations 1 and 2 can accentuate any difference between the values specified by the mathematical functions Feature(beat) and Feature(beat+[N]). The inverted polarity of the differences between the first and second groups is illustrated in FIGS. 15-17 where the direction of the dotted-line arrows that represent the difference features Q alternates between adjacent difference features Q.

[0063]   The feature map provides a visual indication of the divergence of the two groups of points, and thus the existence of a significant alternans pattern of variation. If there is a significant ABAB... alternans pattern of variation, the two groups of points will show separate clusters on the feature map (for example, as shown in FIGS. 20 and 22). If there is not a significant ABAB... alternans pattern of variation, the feature map will illustrate a more random pattern of points from the two groups (for example, as shown in FIG. 21).

[0064]   FIGS. 18 and 19 illustrate two examples of feature maps. The [E] points plotted to generate the feature maps of FIGS. 18 and 19 were determined using ECG data representative of an ECG signal having a 5 microvolt TWA pattern of variation, 20 microvolts of noise, and 20 milliseconds of offset, where [H] is equal to 128. The first and second groups of points can be distinguished by the markers utilized to represent the points of the group (i.e., the first group of points, group A, can include asterisks shaped markers, and the second group of points, group B, can include round markers). Lines can be used to connect sequential markers of each group (e.g., for group A, point-two P_{2A} can be connected to each of point-one P_{1A} and point-three P_{3A} by lines).

[0065]   The feature map of FIG. 18 illustrates a plot of points determined using values directly from the feature matrix A (i.e., the feature matrix A was not preprocessed using a principal component analysis or other mathematical analysis). As illustrated in FIG. 18, the points of the first and second groups are intermixed (i.e., the feature map illustrates a random pattern of the points from the two groups). Accordingly, the feature map of FIG. 18 does not

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illustrate the presence of a significant divergence of the two groups of points, and thus, does not indicate the existence of a significant alternans pattern of variation.

[0066]   The feature map of FIG. 19 illustrates a plot of points determined using values of a first principal vector u_1. The first principal vector u_1 is a result of a principal component analysis performed on the same feature matrix A from which the values used to determine the points L plotted in FIG. 18 were obtained. As illustrated in FIG. 19, although the first and second groups of points are partially overlapped, the first group of points is primarily positioned in the upper-left quadrant of the feature map and the second group of points is primarily positioned in the lower-right quadrant of the feature map. Accordingly, the feature map of FIG. 19 appears to illustrate the presence of a significant divergence of the two groups of points, and thus, a significant alternans pattern of variation may exist.

[0067]   Although FIGS. 18 and 19 illustrate the same ECG data, the feature map of FIG. 19 indicates the existence of an alternans pattern of variation, while the feature map of FIG. 18 does not. The effect of noise and time shift in the measured ECG signal on the determined alternans data is clearly indicated by the feature maps of FIGS. 18 and 19. Preprocessing the feature matrix A increases the robustness of the determination of alternans data by limiting the effect of noise and time shift in the measured ECG signal.

[0068]   In some embodiments, multiple feature maps can be generated for various quantities of [N] using the same set of values (e.g., the feature maps for [N]=1, 2, and 3, respectively, can be generated using the points determined in Tables 1-3). The display of multiple feature maps can further verify the existence of a significant alternans pattern of variation for the proposed alternans pattern of variation (e.g., a ABAB... alternans pattern of variation).

[0069]   FIGS. 20-22 illustrate feature maps for [N]=1, 2, and 3, respectively, where the points plotted in each of the feature maps were determined using the same set of values. The divergence of the first and second groups of points in the feature maps of FIGS. 20 and 22 in combination with the lack of divergence of the first and second groups of points in the feature map of FIG. 21 provides visual evidence that the proposed ABAB... alternans pattern of variation is correct.

[0070]   The operator can change the proposed alternans pattern of variation (i.e., change the grouping of the points to a different alternans pattern of variation) if the feature maps for

[N]=1, 2, and 3 do illustrate differing divergence patterns for [N]=1 and 3 and [N]=2, respectively. For example, if the two groups of points diverge in the feature map for [N]=1 and 2, but not for the feature maps of [N]= 3, the ECG signal represented by the values used to determine the points for the feature maps does not represent the proposed ABAB... alternans pattern of variation. However, the ECG signal can include a different alternans pattern of variation. Reassignment of the [E] points to different groups can be used to test a different proposed alternans pattern of variation.

[0071]   As shown in FIG. 3, the processor (at 112) can statistically analyze the data plotted in the feature map. Although the feature map provides a visual indication of the existence of a significant alternans pattern of variation, the feature map does not provide a quantitative measure of the confidence level of the alternans pattern of variation. Accordingly, the data plotted in the feature map, or similar types of data that are not plotted in a feature map, can be statistically analyzed to provide such quantitative measures of the confidence level of the alternans pattern of variation.

[0072]   In some embodiments, a paired T-test can be performed on the first and second groups of points. A paired T-test is a statistical test which is performed to determine if there is a statistically significant difference between two means. The paired T-test can provide a p-value (e.g., p=0.001). In one embodiment, the confidence level is increased (i.e., a significant alternans pattern of variation exists) when the p-value is less than 0.001. In other embodiments, other suitable threshold levels can be established.

[0073]   In some embodiments, a cluster analysis (e.g., a fuzzy cluster analysis or a K-mean cluster analysis) can be performed on the [E] points to determine a first cluster of points and a second cluster of points. The cluster analysis can also generate a first center point for the first cluster and a second center point for the second cluster. The first and second clusters of points can be compared with the first and second groups of points, respectively. A determination can be made of the number of clustered points that match the corresponding grouped points. For example, if point-one L_1 and point-two L_2 are clustered in the first cluster, point-three L_3 and point-four L_4 are clustered in the second cluster, point-one L_1, point-two L_2, and point-three L_3 can be grouped in the first group, and point-four L_4 can be grouped in the second group. Clustered point-three L_3 does not correspond to grouped point-three L_3, thereby resulting in a 75% confidence level. The confidence level can represent the percentage of clustered points that match the corresponding grouped points. In one

embodiment, a confidence level about 90% can be a high confidence level, a confidence level between 60% and 90% can be a medium confidence level, and a confidence level below 60% can be a low confidence level. In other embodiments, the thresholds for the high, medium, and/or low confidence levels can be other suitable ranges of percentages or values.

[0074]   As shown in FIG. 3, the processor can determine (at 114) an estimate of an amplitude of the alternans pattern of variation. As discussed above, in one embodiment, the square-root of a principal component (e.g., the first principal component S_1) can be used to provide an estimate of the amplitude. In other embodiments, a distance can be determined between a first center point of a first group of points and a second center point of a second group of points. The center points can include the center points of the first and second groups of points A and B as determined using a mathematical analysis (e.g., by taking the mean or median of the values of the points for each respective group), the center points provided by the Paired T-test, the center points provided by the cluster analysis, or any other determined center points that represent the ECG data.

[0075]   FIG. 23 illustrates a distance measurement between the first and second center points. The distance can be determined using Equation 9 shown below, where the first center point includes an X-value X_1 and a Y-value Y_1 and the second center point includes an X-value X_2 and a Y-value Y_2.

$$[e9] \quad \text{Amplitude}_{\text{ESTIMATE}} = \sqrt{(X_1 - X_2)^2 + (Y_1 - Y_2)^2}$$

[0076]   The amplitude of the alternans pattern of variation often depends on the [D] morphology features used to determine the values W. Accordingly, the estimated amplitude is generally not an absolute value that can be compared against standardized charts. However, comparisons can be generated for estimated amplitudes of alternans patterns of variation based on the morphology features F that are determined and the processing step that is used.

[0077]   As shown in FIG. 3, the processor can report (at 116) alternans data to a caregiver and/or the processor can store the alternans data. The alternans data (e.g., the feature maps, the estimated amplitudes of the alternans pattern of variation, the confidence level of the alternans pattern of variation, the uncertainty level of the alternans pattern of variation, the p-

value of the alternans pattern of variation, and the like) can be reported using any suitable means (e.g., output to a suitable output device such as a display, a printer, and the like).

[0078]   As shown in FIG. 3, in some embodiments, the processor can plot (at 118) a spectral graph using values resulting from preprocessing the feature matrix (e.g., the values of the first principal component vector u_1). FIGS. 24 and 25 illustrate two examples of spectral graphs. The values used to generate the spectral graphs of both FIGS. 24 and 25 were determined using ECG data representative of an ECG signal having a 5 microvolt TWA pattern of variation, 20 microvolts of noise, and 20 milliseconds of offset, where [H] is equal to 128.

[0079]   FIG. 24 illustrates a spectral graph generated using values directly from the feature matrix A (i.e., the feature matrix A was not preprocessed using a principal component analysis or other mathematical analysis). As illustrated in FIG. 24, the spectral graph does not include a dominant frequency at half of the beat sample frequency, but instead includes a number of frequency spikes having varying amplitudes. Accordingly, the spectral graph of FIG. 24 does not indicate the existence of a significant alternans pattern of variation. FIG. 25 illustrates a spectral graph generated using values of a first principal vector u_1. The first principal vector u_1 is a result of a principal component analysis performed on the same feature matrix A from which the values used to generate the spectral graph of FIG. 24 were obtained. FIG. 25 illustrates a single frequency spike at half of the beat sample frequency. Accordingly, unlike the spectral graph of FIG. 24, the spectral graph of FIG. 25 appears to illustrate the presence of a significant alternans pattern of variation. The effect of noise and time shift in the measured ECG signal on the determined alternans data is indicated by the spectral graphs of FIGS. 24 and 25. Preprocessing the feature matrix A increases the robustness of the determination of alternans data when using spectral domain methods.